JOC*Note*

Domino Michael−Aldol Reactions on 1,4-Diarylbut-2-ene-1,4-diones with Methyl Acetoacetate Furnish Methyl 2-Aroyl-4-hydroxy-6-oxo-4-arylcyclohexane-1-carboxylate Derivatives†

H. Surya Prakash Rao* and S. P. Senthilkumar

Department of Chemistry, Pondicherry University, Pondicherry 605 014, India

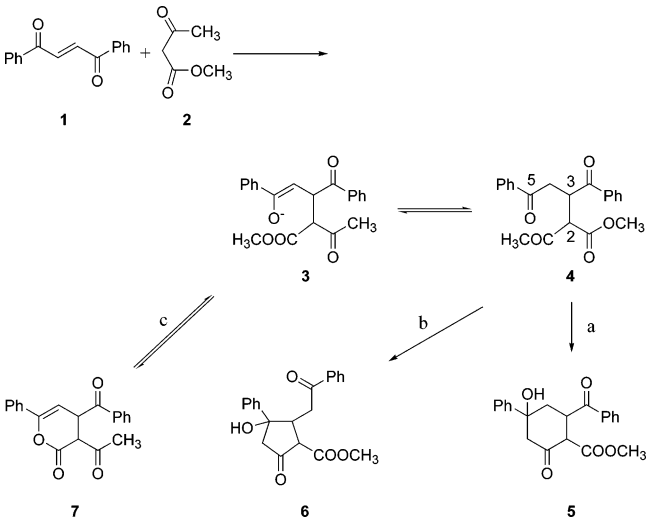
hspr@yahoo.com

Received September 22, 2003

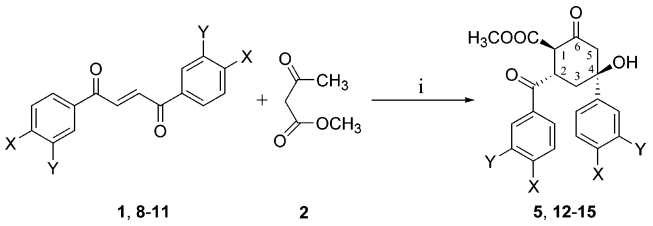
Abstract: Domino Michael-Aldol reactions on 1,4-diaryl-2-butene-1,4-diones with methyl acetoacetate in the presence of activated $Ba(OH)_2$ furnished methyl (1*R**,2*S**,4*S**)-2-aroyl-4-hydroxy-6-oxo-4-arylcyclohexane-1-carboxylate derivatives in a stereo- and regiospecific manner. While treatment of these cyclohexanecarboxylate products with TsOH resulted in the dehydrated and decarbomethoxylated cyclohexenone derivatives, the reaction with NaOMe furnished 3,5-disubstituted phenols via dehydration, decarbomethoxylation, and dehydrogenation. NaCl/DMSO under microwave irradiation transformed the cyclohexanecarboxylate products to the 7-hydroxyisobenzofuranone derivatives.

The domino processes involving Michael-Aldol-dehydration reactions on an α,*β*-unsaturated carbonyl compound with active methylene ketones is a well-known one-flask protocol for generating six-membered rings.[1] This sequence, when applied to cyclic ketones, is a classical reaction called Robinson annulation.[2] Even though the method has enormous scope and is widely applied for the condensation of active methylene species with different ketones and α,*β*-unsaturated ketones, surprisingly it has never been attempted on acyclic 2-ene-1,4-diones. The 2-ene-1,4-diones, e.g., *trans*-1,4-diphenylbut-2-ene-1,4-dione (*trans*-DBE) **1**, are interesting substrates for the study of this useful transformation as there are two carbonyl groups conjugated to a common double bond. Initial reaction of **1** with an active methylene compound such as methyl acetoacetate (methyl 3-oxobutanoate; MAA) **2** should occur through Michael addition to furnish methyl 2-acetyl-3-benzoyl-5-oxo-5-phenylpentanoates **4** via enolate **3** (Scheme 1). Subsequently, the reaction sequence may follow intramolecular aldol condensation involving C-2 acetyl and C-5 carbonyl groups (route a, Scheme 1) leading to the formation of the cyclohexanecarboxylate derivatives **5**. On the other hand, reaction may go through intramolecular aldol condensation involving C-2 acetyl and C-3 benzoyl groups (route b, Scheme 1) to furnish cyclopentanone derivatives **6**. It is also possible that initially formed enolate **3** may undergo cyclization leading to the formation of lactone **7** (route c, Scheme 1). In recent years, we have studied the domino reactions of *trans*-DBE and its derivatives with active methylene compounds,[3] and in continuation of this study and to test the above possibilities, we have now conducted $Ba(OH)_2$-mediated condensation reactions on *trans*-DBE **1** and its derivatives with MAA **2**.

SCHEME 1



SCHEME 2[a]



1, **5**: X = Y = H; **8**, **12**: X = Cl, Y = CH_3; **9**, **13**: X = Br, Y = H; **10**, **14**: X = CH_3, Y = H; **11**, **15**: X = OCH_3, Y = H.

[a] Reagents and conditions: (i) activated $Ba(OH)_2$, MeOH or 3:2 MeOH/$CHCl_3$, rt, 12 h.

When *trans*-DBE **1** was treated with MAA **2** in the presence of activated $Ba(OH)_2$ in methanol, the reaction furnished methyl (1*R**,2*S**,4*S**)-2-benzoyl-4-hydroxy-6-oxo-4-phenylcyclohexane-1-carboxylate **5** as a single diastereomer exclusively in about 60% yield (Scheme 2). The structure and stereochemistry of the cyclohexanecarboxylate **5** (mp 152−154 °C) was confirmed on the basis of spectral (IR, ^{1}H NMR, ^{13}C NMR, DEPT, COSY, NOESY, and MS) data and elemental analysis. The stereochemistry of the different substituents was assigned on the basis of vicinal and long-range couplings as well as NOESY data.

To test the generality of the above reaction, (*E*)-1,4-di(4-chloro-3-methylphenyl)-2-butene-1,4-dione **8**, (*E*)-1,4-di(4-bromophenyl)-2-butene-1,4-dione **9**, (*E*)-1,4-di(4-methylphenyl)-2-butene-1,4-dione **10**, and (*E*)-1,4-di(4-methoxyphenyl)-2-butene-1,4-dione **11** were reacted with MAA **2** in the presence of activated $Ba(OH)_2$. The

† Dedicated to Professor Hans W. Scheeren on the occassion of his 65th birthday.

(1) (a) Rapson, W. S.; Robinson, R. *J. Chem. Soc.* **1935**, 1285. (b) Gawley, R. E. *Synthesis* **1976**, 777.

(2) (a) Wilds, A. L.; Shunk, C. H. *J. Am. Chem. Soc.* **1943**, *65*, 469. (b) Johnson, W. S.; Szmuszkovicz, J.; Miller, M. *J. Am. Chem. Soc.* **1950**, *72*, 3726.

(3) Rao, H. S. P.; Senthlkumar, S. P. *Ind. J. Chem.*, in press.

10.1021/jo0353839 CCC: $27.50
Published on Web 03/05/2004

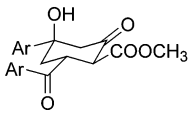


FIGURE 1.

reactions of **8**−**10** furnished the corresponding cyclohexanecarboxylates **12**−**14** in about 54−65% yield as single diastereomers (Scheme 2). However, in the case of **11**, the cyclohexanecarboxylate **15** was obtained as a mixture of isomers in 54% yield. Structures were assigned to the cyclohexanecarboxylates **12**−**15** on the basis of spectral data, which matched well with the parent compound **5**.

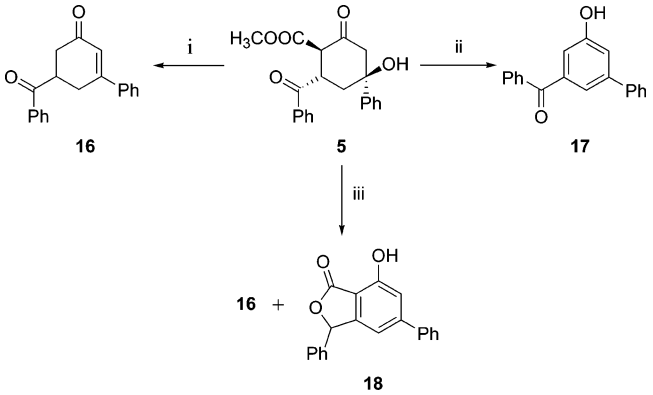
The mechanism of formation and the stereochemistry of cyclohexanecarboxylate **5** deserve comment here. The initial Michael addition of the anion from methyl acetoacetate **2** would generate enolate anion **3**. Under the reaction conditions the lactone **7** (route c, Scheme 1) formed by cyclization is likely to be in equilibrium with the enolate anion **3**. On the other hand, the triketoester **4** generated from **3** undergoes irreversible intramolecular aldol condensation involving C-2 acetyl and C-5 carbonyl groups leading to the formation of **5** (route a, Scheme 1). The formation of **5** instead of **6** from acyclic triketone precursor **4** was following the expected pathway (a, Scheme 1) as predicted by Baldwin rules.[4]

The stereochemistry of the ester group in **5** reflects stable equatorial orientation generated via keto−enol tautomerism of the β-ketoester moiety in **5** (Figure 1). The relative cis stereochemistry of C-2 benzoyl group and C-4 phenyl group would arise from the penultimate aldol condensation step and reflects stable equatorial orientation of the bulky phenyl and benzoyl groups (Figure 1). Thus, not surprisingly out of four possible pairs of diastereomers, single pair of diasteriomeric products **5** and **12**−**14** were formed in the reaction.

Generally, the final products in the domino reactions involving α,β-unsaturated carbonyl compounds and MAA are enones.[5] However, surprisingly in the present case the reaction stopped at the cyclohexanol stage and the expected dehydration step did not take place. When the cyclohexanecarboxylate **5** was subjected to dehydration with *p*-TSA in refluxing benzene, using a Dean−Stark apparatus, the reaction furnished known[6] 5-benzoyl-3-phenyl-2-cyclohexen-1-one **16** in 96% yield (Scheme 3). The product **16** was formed via a dehydration and decarbomethoxylation sequence.

The cyclohexanecarboxylate **5** was treated with NaOMe in MeOH with the intention of effecting dehydration while keeping the ester moiety intact. However, surprisingly, this reaction furnished the known[7] 3,5-disubstituted phenol **17** (Scheme 3). In this transformation, loss of ester and water were taking place with concomitant dehydrogenative aromatization. Polysubstituted phenols of the type **17** have found use as precursors to the corresponding quinones, which exhibit biocide properties.[8]

SCHEME 3[a]



[a] Reagents and conditions: (i) *p*-TSA, benzene, Dean−Stark, reflux, 5 h, 96%; (ii) NaOMe, MeOH, rt, 17 h, 91%; (iii) DMSO/NaCl, $\mu\nu$, 650W, 5 min.

When the decarbomethoxylation reaction of **5** was conducted using DMSO/NaCl[9] under microwave irradiation, the reaction furnished 7-hydroxy-3,5-diphenyl-1,3-dihydro-1-isobenzofuranone **18** (53%, mp 156−158 °C) along with the cyclohexenone **16** (23%, mp 106−108 °C; Scheme 3). In the ^{1}H NMR spectrum of 7-hydroxyisobenzofuranone **18**, the C-3-H appeared as a characteristic singlet at 6.40δ. Interestingly, **18** appears as a structural motif in a few natural products such as bassidifferquinone A and bassidifferquinone B.[10] These phenolic compounds are produced by *Streptomyces* sp. B-412 and found to induce fruiting body formation in *Favolus arcularius*.

A possible mechanism for the formation of the 1,3-dihydroisobenzofuranone **18** is given in Scheme 4. Dehydration of the *tert*-alcohol **5** would lead to **19**, which would undergo aromatization to **21** via the enol form **20**. Further lactonization of **21** would then furnish 7-hydroxy-3,5-diphenyl-1,3-dihydro-1-isobenzofuranone **18**.

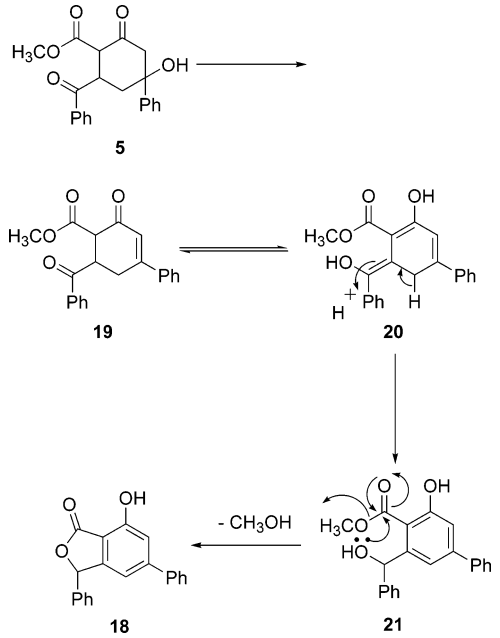
In summary, we have shown that $Ba(OH)_2$-mediated condensation of *trans*-DBE **1** and its derivatives **8**−**11** with MAA **2** furnishes cyclohexanecarboxylates **5**, **12**−**15** exclusively. While attempted dehydration of **5** with *p*-TSA led to dehydrated and decarbomethoxylated product **16**, the reaction with NaOMe furnished dehydrated, decarbomethoxylated and dehydrogenated product, 3,5-disubstituted phenol **17**. On the other hand, the microwave-mediated decarbomethoxylation of **5** with NaCl/DMSO furnished 7-hydroxyisobenzofuranone **18**.

Experimental Section

Condensation Reactions of (*E*)-1,4-Diphenyl-2-butene-1,4-dione (1) with MAA (2). To a well-stirred suspension of activated $Ba(OH)_2$ (145 mg, 0.85 mmol) in dry methanol (10 mL) was added MAA **2** (541 mg, 4.66 mmol), and the mixture was allowed to stir at room temperature for 15 min. Then, *trans*-DBE **1** (1.0 g, 4.24 mmol) was added in portions, and stirring

(4) Baldwin, J. E.; Lusch, M. J. *Tetrahedron* **1982**, *38*, 2939.
(5) Iglesias, M.; Marinas, J. M.; Sinisterra, J. V. *Tetrahedron* **1987**, *43*, 2335.
(6) Kitano, H.; Minami, S.; Morita, T.; Matsumoto, K.; Hatanaka, M. *Synthesis* **2002**, *6*, 739.
(7) Katritzky, A. R.; Ji, Y.; Tymoshenko, D. O.; Fang, Y.; Hylton, K.-G. *ARKIVOC* **2001**, *iv*, 20.
(8) (a) Bergeron, D.; Brassard, P. *Heterocycles* **1992**, *34*, 1835. (b) Brimble, M. A.; Phythian, S. J. *Tetrahedron Lett.* **1993**, *34*, 5813. (c) Magnus, P.; Eisenbeis, S. A.; Magnus, N. A. *J. Chem. Soc., Chem. Commun.* **1994**, 1545. (d) Nicolaou, K. C.; Gross, J. L.; Kerr, M. A.; Lemus, R. H.; Ikeda, K.; Ohe, K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 781.
(9) (a) Krapcho, A. P. *Synthesis* **1982**, 805. (b) Krapcho, A. P.; Lovey, A. J. *Tetrahedron Lett.* **1973**, 957.
(10) Azuma, M. *Agric. Biol. Chem.* **1990**, *54*, 1441.

SCHEME 4



was continued for 12 h. The reaction mixture turned to reddish brown. On completion of the reaction (TLC), the solid suspension was filtered through a Celite pad and the filtrate was concentrated in vacuo to about 3 mL. The reaction mixture was then diluted with dichloromethane (40 mL) and poured over ice-cooled water. The organic layer was separated, washed again with water (3 × 30 mL) and brine solution (2 × 10 mL), and dried over anhydrous Na_2SO_4. Removal of solvent resulted in a reddish brown viscous liquid, which was loaded on a column of silica gel (1 cm × 20 cm, 100−200 mesh) and eluted with hexane/ethyl acetate (85:15) to furnish methyl (1*R**,2*S**,4*S**)-2-benzoyl-4-hydroxy-6-oxo-4-phenylcyclohexane-1-carboxylate **5** (599 mg, 60%) as a colorless solid.

Methyl (1*R,2*S**,4*S**)-2-benzoyl-4-hydroxy-6-oxo-4-phenylcyclohexane-1-carboxylate (5):** colorless solid; mp 152−154 °C; R_f = 0.22 (80:20 hexane/ethyl acetate); IR (KBr) 3409, 2998, 1732, 1703, 1663, 1595, 1449, 1368, 1269, 1163, 1017, 986, 752, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.15 (t, J = 13.5 Hz, 1H), 2.38 (dt, J = 16.5, 2.5 Hz, 1H), 2.73 (dd, J = 14.0, 2.5 Hz, 1H), 3.10 (d, J = 14.0 Hz, 1H), 3.72 (s, 3H), 4.19 (d, J = 12.0 Hz, 1H), 4.83 (td, J = 13.0, 4.0 Hz, 1H), 7.26−7.30 (m, 2H), 7.36 (t, J = 7.5 Hz, 2H), 7.43−7.49 (m, 3H), 7.58 (dt, J = 8.0 Hz, 1.5, 1H), 8.03 (d, J = 8.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$/CCl_4) δ 41.6, 44.3, 52.3, 54.0, 57.9, 77.2, 124.3, 127.9, 128.8, 128.9 (2C), 133.6, 135.2, 145.5, 169.4, 199.9, 203.9; LRMS 352 (M^+, did not appear), 334 (7), 247 (31), 215 (20), 173 (11), 120 (12), 105 (100), 77 (79), 51 (13).; Anal. Calcd for $C_{21}H_{20}O_5$ C, 71.58; H, 5.72. Found: C, 71.28, H, 6.35.

Reaction of (*E*)-1,4-Di(4-chloro-3-methylphenyl)-2-butene-1,4-dione (8) and MAA (2). Following the general procedure described above, activated $Ba(OH)_2$ (58 mg, 0.34 mmol), MAA **2** (214 mg, 1.85 mmol), and (*E*)-1,4-di(4-chloro-3-methylphenyl)-2-butene-1,4-dione **8** (500 mg, 1.68 mmol) in 10 mL of 3:2 MeOH/$CHCl_3$ gave methyl 2-(4-chloro-3-methylbenzoyl)-4-(4-chloro-3-methylphenyl)-4-hydroxy-6-oxocyclohexane-1-carboxylate **12** (371 mg, 54%) after purification by column chromatography.

Methyl 2-(4-chloro-3-methylbenzoyl)-4-(4-chloro-3-methylphenyl)-4-hydroxy-6-oxocyclohexane-1-carboxylate (12): viscous oil; R_f = 0.25 (80:20 hexane/ethyl acetate); IR (KBr) 3480, 2954, 2854, 1743, 1715, 1641, 1593, 1569, 1480, 1445, 1377, 1340, 1216, 1165, 1048, 894, 760, 698, 615 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.10 (t, J = 13.64, 1H), 2.31 (s, 1H), 2.33 (s, 3H), 2.39 (s, 3H), 2.70 (dd, J = 13.84, 2.08 Hz, 1H), 3.05 (d, J = 13.84 Hz, 1H), 3.68 (s, 3H), 4.15 (d, J = 11.72 Hz, 1H), 4.74 (td, J = 12.36, 3.64 Hz, 1H), 7.19 (t, J = 6.16 Hz, 1H), 7.29 (dt, J = 17.7, 7.52 Hz, 2H), 7.42 (t, J = 8.32 Hz, 1H), 7.77 (d, J = 6.48 Hz, 1H), 7.85 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.60, 20.13, 41.27, 44.28, 52.46, 53.75, 57.80, 76.76, 123.1, 126.9, 127.5, 129.3, 129.7, 131.1, 133.4, 136.4, 137.0, 140.6, 143.9, 169.6, 199.6, 204.3; LRMS 448 (M^+, 2), 430 (4), 363 (2), 277 (20), 263 (12), 245 (14), 219 (12), 189 (4), 153 (100), 125 (26), 105 (5), 89 (10), 69 (4). Anal. Calcd for $C_{23}H_{22}Cl_2O_5$: C, 61.48; H, 4.94. Found: C, 61.52; H, 4.99.

Reaction of (*E*)-1,4-Di(4-bromophenyl)-2-butene-1,4-dione (9) with MAA (2). Following the general procedure described above, activated $Ba(OH)_2$ (43 mg, 0.25 mmol), MAA **2** (162 mg, 1.4 mmol), and (*E*)-1,4-di(4-bromophenyl)-2-butene-1,4-dione **9** (500 mg, 1.27 mmol) in 10 mL of 3:2 MeOH/$CHCl_3$ gave methyl (1*R**,2*S**,4*S**)-2-(4-bromobenzoyl)-4-(4-bromophenyl)-4-hydroxy-6-oxocyclohexane-1-carboxylate **13** (427 mg, 61%) as a colorless solid after purification by column chromatography.

Methyl (1*R,2*S**,4*S**)-2-(4-bromobenzoyl)-4-(4-bromophenyl)-4-hydroxy-6-oxocyclohexane-1-carboxylate (13):** colorless solid; mp 160−162 °C; R_f = 0.26 (80:20 hexane/ethyl acetate); IR (KBr) 3462, 2925, 2854, 1733, 1715, 1681, 1584, 1458, 1377, 1257, 1226, 1166, 1072, 1009, 822, 740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (t, J = 13.36 Hz, 1H), 2.30 (dt, J = 18.0, 6.0 Hz, 1H), 2.70 (dd, J = 13.92, 2.32 Hz, 1H), 3.04 (s, 1H), 3.05 (d, J = 10.6 Hz, 1H), 3.71 (s, 3H), 4.15 (d, J = 11.72 Hz, 1H), 4.73 (td, J = 12.44, 3.72 Hz, 1H), 7.31 (d, J = 8.56 Hz, 2H), 7.47 (d, J = 8.52 Hz, 2H), 7.61 (d, J = 8.44 Hz, 2H), 7.86 (d, J = 8.52 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.3, 44.2, 52.6, 53.7, 57.8 76.9, 122.1, 126.1, 129.2, 130.3, 131.9, 132.3, 133.7, 144.2, 169.4, 199.2, 203.7; FAB-MS 511 (M^+ + 1). Anal. Calcd for $C_{21}H_{18}O_5Br_2$: C, 49.44; H, 3.56. Found: C, 49.44; H, 3.17.

Reaction of (*E*)-1,4-Di(4-methylphenyl)-2-butene-1,4-dione (10) and MAA (2). Following the general procedure described above, activated $Ba(OH)_2$ (68 mg, 0.4 mmol), MAA **2** (255 mg, 2.2 mmol), and (*E*)-1,4-di(4-methylphenyl)-2-butene-1,4-dione **10** (528 mg, 2 mmol) in 10 mL of MeOH gave methyl (1*R**,2*S**,4*S**)-2-(4-methylbenzoyl)-4-(4-methylphenyl)-4-hydroxy-6-oxocyclohexane-1-carboxylate **14** (513 mg, 65%) as a colorless solid after purification by column chromatography.

Methyl (1*R,2*S**,4*S**)-4-hydroxy-2-(4-methylbenzoyl)-4-(4-methylphenyl)-6-oxocyclohexane-1-carboxylate (14):** colorless solid; mp 158−160 °C; R_f = 0.3 (80:20 hexane/ethyl acetate); IR (KBr) 3402, 2922, 1749, 1712, 1670, 1604, 1568, 1517, 1462, 1435, 1379, 1340, 1265, 1235, 1186, 1169, 1127, 1076, 1041, 1016, 978, 843, 817, 766, 736 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (t, J = 12.84 Hz, 1H), 2.30 (s, 3H), 2.34 (dt, J = 18.0, 7.0 Hz, 1H), 2.39 (s, 3H), 2.71 (dd, J = 13.88, 2.32 Hz, 1H), 2.86 (s, 1H), 3.05 (d, J = 13.8 Hz, 1H), 3.69 (s, 3H), 4.16 (d, J = 11.72 Hz, 1H), 4.79 (td, J = 12.44, 3.6 Hz, 1H), 7.14 (d, J = 8.12 Hz, 2H), 7.25 (d, J = 8.04 Hz, 2H), 7.31 (d, J = 8.16 Hz, 2H), 7.92 (d, J = 8.2 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 21.7, 41.6, 44.3, 52.3, 54.0, 57.9, 77.1, 124.1, 128.9, 129.4, 129.6, 132.5, 137.7, 142.5, 144.7, 169.6, 199.9, 204.5 ppm; FAB-MS 381 (M^+ + 1). Anal. Calcd for $C_{23}H_{24}O_5$: C, 72.79; H, 7.82. Found: C, 72.51, H, 7.82.

Reaction of (*E*)-1,4-Di(4-methoxyphenyl)-2-butene-1,4-dione (11) with MAA (2). Following the general procedure described above, activated $Ba(OH)_2$ (58 mg, 0.34 mmol), MAA **2** (215 mg, 1.85 mmol), and (*E*)-1,4-di(4-methoxyphenyl)-2-butene-1,4-dione **11** (500 mg, 1.68 mmol) in MeOH (10 mL) gave methyl (1*R**,2*S**,4*S**)-2-(4-methoxybenzoyl)-4-(4-methoxyphenyl)-4-hydroxy-6-oxocyclohexane-1-carboxylate **15** (371 mg, 54%) as a colorless solid after purification by column chromatography.

Methyl (1*R,2*S**,4*S**)-4-hydroxy-2-(4-methoxybenzoyl)-4-(4-methoxyphenyl)-6-oxocyclohexane-1-carboxylate (15):** colorless solid; mp 142−144 °C; R_f = 0.27 (70:30 hexane/ethyl acetate); IR (KBr) 3455, 2922, 2853, 1743, 1719, 1651, 1599, 1511, 1463, 1261, 1161, 1022, 976, 846 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.12 (t, J = 13.4 Hz, 1H), 2.35 (dt, J = 18.76, 6.25 Hz, 1H), 2.39 (s, 1H), 2.72 (dd, J = 13.8, 2.44 Hz, 1H), 3.05 (d, J = 13.76 Hz, 1H), 3.72 (s, 3H), 3.78 (s, 3H), 4.15 (d, J = 11.76 Hz, 1H), 4.74 (td, J = 12.6, 3.72 Hz, 1H), 6.87 (d, J = 8.88 Hz, 2H), 6.94 (d, J = 8.92 Hz, 2H), 7.34 (d, J = 8.88 Hz, 2H), 8.01 (d, J = 8.92 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.8, 43.9, 52.4, 54.1, 55.3, 55.5, 58.0, 77.0, 114.1 (2C), 125.4, 128.0, 131.2, 137.6,

164.1, 169.5, 198.5, 204.1; FAB-MS 413 ($M^+ + 1$). Anal. Calcd for $C_{23}H_{24}O_7$: C, 66.98; H, 5.87. Found: C, 66.95; H, 5.91.

Reaction of Methyl (1*R,2*S**,4*S**)-2-Benzoyl-4-hydroxy-6-oxo-4-phenylcyclohexane-1-carboxylate (5) with *p*-TSA.** To methyl (1*R**,2*S**,4*S**)-2-benzoyl-4-hydroxy-6-oxo-4-phenylcyclohexane-1-carboxylate **5** (120 mg, 0.34 mmol) taken in dry benzene (5 mL) was added a catalytic amount of *p*-TSA (2 mg), and the reaction mixture was allowed to reflux for 5 h in a reaction vessel having Dean−Stark setup. After completion of the reaction (TLC), the reaction mixture was concentrated in vacuo to 2 mL. The reaction mixture was then diluted with dichloromethane (20 mL) and poured over ice-cooled water. The organic layer was separated, washed further with water (3 × 5 mL) and brine solution (1 × 5 mL), and finally dried over anhydrous Na_2SO_4. The brown viscous liquid obtained on removal of the solvent was subjected to column chromatography (silica gel 100−200 mesh) and furnished 5-benzoyl-3-phenyl-2-cyclohexen-1-one **16** (90 mg, 96%) as a colorless solid.

5-Benzoyl-3-phenyl-2-cyclohexen-1-one (16): colorless solid; mp 106−108 °C (lit.[5] mp 107−108 °C); R_f = 0.47 (80:20 hexane/ethyl acetate); IR (KBr) 3060, 2950, 1676, 1600, 1577, 1494, 1446, 1353, 1257, 1161,1031, 999, 925, 892759, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$/ CCl_4) δ 2.67 (t, J = 11.4 Hz, 2H), 2.93 (dd, J = 4.5, 13.5 Hz, 1H), 3.64 (qd, 1H), 6.42 (d, J = 2.4 Hz, 1H), 7.37 (t, J = 3.3 Hz, 3H), 7.46−7.57 (m, 5H); 7.98 (d, J = 4.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$/ CCl_4) δ 30.56, 39.71, 42.46, 125.00, 126.12, 128.45, 128.80, 128.90, 130.13, 133.46, 135.18, 138.29, 157.09, 196.47, 198.96; LRMS 276 (M^+, 4), 197 (8), 171 (100), 153 (8), 141 (12), 128 (16), 115 (18), 105 (100), 77 (44), 51 (8).

Reaction of Methyl (1*R,2*S**,4*S**)-2-Benzoyl-4-hydroxy-6-oxo-4-phenylcyclohexane-1-carboxylate (5) with NaOMe in MeOH.** To methyl (1*R**,2*S**,4*S**)-2-benzoyl-4-hydroxy-6-oxo-4-phenylcyclohexane-1-carboxylate **5** (75 mg, 0.21 mmol) in dry MeOH (3 mL) was added NaOMe (12 mg, 0.21 mmol), and the reaction mixture was stirred at rt for 17 h. After completion of the reaction (TLC), the reaction mixture was concentrated in vacuo to 0.5 mL. The reaction mixture was then diluted with dichloromethane (10 mL) and poured over ice-cooled water. The organic layer was separated, washed further with water (3 × 5 mL), brine solution (2 × 5 mL), and finally dried over anhydrous Na_2SO_4. The brown viscous liquid obtained on removal of the solvent was subjected to column chromatography (silica gel 100−200 mesh) using 85:15 hexane/ethyl acetate as an eluent furnished (5-hydroxybiphenyl-3-yl)phenylmethanone **17** (53 mg, 91%) as a colorless solid.

(5-Hydroxybiphenyl-3-yl)phenylmethanone (17): colorless solid; mp 74−76 °C (lit.[6] mp 76−77 °C; R_f = 0.32 (85:15 hexane/ethyl acetate); IR (KBr) 3348, 3062, 2940, 2863, 1648, 1593, 1421, 1340, 1257, 1006, 873, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (br s, 2H), 7.37 (br d, J = 7.20 Hz, 1H), 7.43 ((t, J = 7.63 Hz, 2H), 7.49 (t, J = 7.76 Hz, 2H), 7.53−7.58 (m, 3H), 7.60 (t, J = 7.44 Hz, 1H), 7.85 (br d, J = 7.13 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.48, 118.39, 121.63, 127.20, 127.98, 128.40, 128.92, 130.17, 132.70, 137.49, 139.55, 139.89, 143.13, 156.23, 196.74; LRMS 274 (M^+, 88), 197 (58), 168 (8), 152 (6), 141 (32), 115 (28), 105 (100), 77 (97), 55 (34), 51 (32).

Microwave-Mediated Reaction of Methyl (1*R,2*S**,4*S**)-2-Benzoyl-4-hydroxy-6-oxo-4-phenylcyclohexane-1-carboxylate (5) with DMSO/ NaCl.** To methyl (1*R**,2*S**,4*S**)-2-benzoyl-4-hydroxy-6-oxo-4-phenylcyclohexane-1-carboxylate **5** (120 mg, 0.34 mmol) dissolved in DMSO (5 mL) was added NaCl (20 mg, 0.34 mmol), and the mixture was subjected to microwave irradiation at 650 W for 3 min. After completion of the reaction (TLC), the reaction mixture indicated the formation of two products. It was cooled to room temperature and diluted with dichloromethane (25 mL). The organic solution was washed with water (5 × 10 mL) and brine solution (1 × 10 mL) and dried over anhydrous Na_2SO_4. The product on removal of solvent was subjected to column chromatography (silica gel 100−200 mesh) with 90:10 hexane/ethyl acetate as eluent to furnish 5-benzoyl-3-phenyl-2-cyclohexen-1-one **16** (22 mg, 23%) and 7-hydroxy-3,5-diphenyl-1,3-dihydro-1-isobenzofuranone **18** (55 mg, 53%).

7-Hydroxy-3,5-diphenyl-1,3-dihydro-1-isobenzofuranone (18): colorless solid; mp 155−158 °C; R_f = 0.15 (80:20 hexane/ethyl acetate); IR (KBr) 3273, 1733, 1615, 1455, 1424, 1326, 1293, 1209, 1084, 1037, 975, 871, 767, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$/ CCl_4) δ 6.40 (s, 1H), 6.95 (s, 1H), 7.14 (s, 1H), 7.30−7.41 (m, 8H), 7.50 (d, J = 6.0 Hz, 2H), 7.81 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$/ CCl_4) δ 109.85, 113.02, 114.83, 127.19, 127.58, 128.77, 129.00, 129.11, 129.51, 136.15, 139.79, 150.43, 151.04, 156.60, 171.49; LRMS 302 (M^+, 50), 197 (100), 168 (10), 139 (12), 115 (16), 105 (38), 77 (36), 51 (12). Anal. Calcd for $C_{20}H_{14}O_3$: C, 79.46; H, 4.67. Found: C, 79.49; H, 4.71.

Acknowledgment. H.S.P.R. thanks UGC, UGC-SAP, and CSIR for financial assistance. S.P.S. thanks CSIR for fellowship. We thank Professor A. Srikrishna, IISc, Bangalore, India, and Professor K. Turnbull, Wright State University, for help.

Supporting Information Available: General experimental details and copies of IR, ^1H NMR, ^{13}C NMR, DEPT, and GC−MS spectra of cyclohexanecarboxylates **5** and **12**−**15**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0353839